P3-096 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Phase II study of erlotinib in chemo-naïve women with advanced pulmonary adenocarcinoma.

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Background: Erlotinib is associated with a survival benefit over placebo for patients with advanced NSCLC who had received 1-2 prior regimens. Its therapeutic role as initial therapy in clinically defined subgroups or in patients prospectively tested for EGFR mutations is less clear.

Methods: Chemotherapy-naïve women with adenocarcinoma, stage IIIB/IV, PS 0-1, who had never smoked or were former smokers, were enrolled and treated with erlotinib 150 mg PO daily, until the time of disease progression or unacceptable toxicity. Response rate was the primary endpoint. Secondary endpoints included overall survival, progression-free survival and toxicity. Tumor tissue adequate for genomic analysis was mandated and prospectively collected for analysis of EGFR and KRAS mutations by direct sequencing.

Results: From 11/04 to 10/06, 40 women were treated. Demographics: median age 65 yrs (range 36-87); 30% PS 0, 70% PS 1; 20% BAC or adenoCA with predominant BAC features, 80% adenoCA without BAC features; smoking status: 63% former, 37 % never. Toxicity: Rash (95%; 30% grade 3) and diarrhea (73%; 10% grade 3) were the most common toxicities. Half of pts developed a toxicity of grade 3 or greater. 5 pts were discontinued due to toxicity, with 2 deaths that were potentially treatment-related: 1 DIC, 1 hepatic failure. There were also two pts with PE's (one fatal). Response: CR 0, PR 12 (30%), SD 11 (28%), and PD 10 (25%), 7 not evaluable. To date, 27 patients have progressed, with 14 deaths. Median PFS was 5.6 months; median overall survival has not yet been reached and exceeds 23 months. Of 32 patients sequenced for EGFR to date, there were 9 exon 19 deletions, 3 L858R mutations, and 1 exon 20 insertion. For the 12 pts prospectively determined to have classic EGFR mutations, RR was 75% (9 PR, 2 SD, 1 not evaluable). Of 15 pts w/ wild-type EGFR, only 1 response (7%) was achieved. The pt with the exon 20 insertion developed PD. Of 28 pts evaluated to date for KRAS, 6 KRAS mutations were found, with no responses in this group (2 PD, 4 SD).

Conclusions: Preliminary results suggest that first-line erlotinib monotherapy may be a useful treatment strategy for women with adenocarcinoma and a limited smoking history. Response rate is particularly impressive for those subjects prospectively found to have an EGFR mutation, and poor for those with KRAS mutations.

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Regressions 14 days following bevacizumab as a single agent as part of neoadjuvant chemotherapy for resectable non-squamous NSCLC

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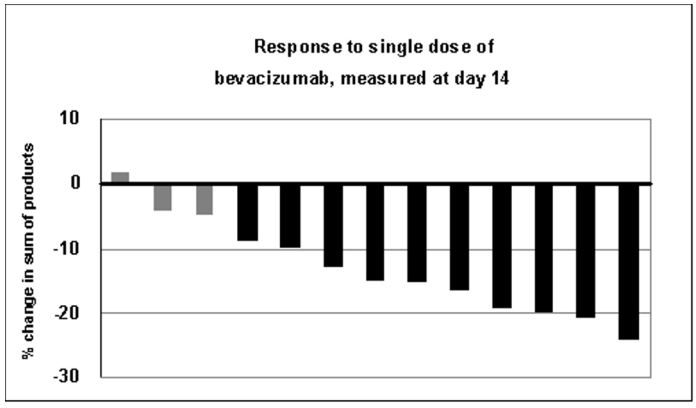
Background: The addition of bevacizumab to standard chemotherapy improves response rate and overall survival in advanced non-squamous NSCLC, but limited data exist on response to treatment with bevacizumab alone. As part of a trial evaluating bevacizumab with docetaxel and cisplatin (DC) as induction therapy for resectable stage IB-IIIA NSCLC, we determined the effect of single agent bevacizumab on tumor size 14 days following a single dose.

Methods: Eligibility was limited to patients with stage IB-IIIA resectable NSCLC. Patients with a contraindication to bevacizumab (squamous histology, central tumor, hemoptysis) received only docetaxel (75 mg/m^2) and cisplatin (75 mg/m^2) q3 weeks for 4 cycles. If patients had no contraindications to bevacizumab, they underwent a baseline CT, a single dose of bevacizumab (15 mg/kg) on day 1, a second CT on day 14, and then 3 cycles of bevacizumab with docetaxel and cisplatin followed by one cycle without bevacizumab. WHO criteria were used to assess response. Following resection, patients in both arms received adjuvant bevacizumab for 1 year.

Results: 22 patients have been enrolled to date. Among the 13 patients who received induction bevacizumab, 10 had IIIA disease, 1 had IIB, and 2 had IB. The average reduction in tumor size (see figure) 14 days after bevacizumab alone was 13% (range +1.6% -24%). Among the 10 who had surgery thus far, 6 had PR. Resections were R0 in 6 patients, R2 in 1, and not resectable for 2; 5 patients were downstaged. During 45 cycles, there has been 1 episode of Grade 2 pre-operative hemoptysis, 1 Grade 3 post-operative GI bleed, and 1 febrile neutropenia. Among patients receiving no induction bevacizumab, 4 had IIIA disease, 1 had IIB, and 3 had IB. All 8 of these patients had had surgery and 6 had PR. Resections were R0 in all cases; 5 were downstaged. The chemotherapy drug delivery was 95% for both preoperative treatment arms.



Conclusions: Treatment with a single dose of bevacizumab causes measurable decrease in tumor size in non-squamous NSCLC. The study is ongoing; we intend to determine the association between 14 day bevacizumab response and downstaging with neoadjuvant bevacizumab/docetaxel/cisplatin, the primary endpoint of the study, to determine whether this measurement might serve as an early marker of biologic effect. Patient accrual continues. Supported by Genentech, Inc.